*REMARKS*

Reconsideration of the pending claims is respectfully requested in view of the foregoing amendments and the following remarks.

*Status of the Application*

Claims 55-108 are under examination, with claims 1-54 previously having been canceled without prejudice.

*Amendments*

Claims 55-100, 107 and 108 are amended. As these amendments are fully supported by the application as filed, no new matter has been introduced in to the application by way of these amendments.

*Summary of the Office Action*

The Office Action rejects claims 99-108 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement.

The Office Action rejects claims 55-108 under 35 U.S.C. § 112, second paragraph, for the use of an allegedly indefinite claim term.

The Office Action rejects claims 59, 61, 62, 64-76, and 79-96 as allegedly obvious over the Du publication in view of U.S. Patents 5,968,943 and 6,407,239 (hereinafter "the Cao '943 patent" and "the Cao '239 patent," respectively) or U.S. Patent 6,040,313 (hereinafter "Wall").

*Discussion of the Enablement Rejection*

The Office Action rejects claims 99-108, directed to the use of the claimed compounds to treat cancer, under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Specifically, the Office Action alleges that because only one cancer cell line (a breast cancer cell line) was used to show the anti-cancer activity of the claimed compounds, the application does not enable the claimed compounds use against "every type of known cancer." Applicants respectfully traverse.

The application discloses the claimed compounds as topoisomerase I inhibitors. *See* application, paragraph [0030]. At the time of the application's effective filing date, topoisomerase I inhibition was known to have broad utility in the treatment of a wide variety

of cancers. Further, as camptothecins, the claimed compounds are members of a long established class of anticancer drugs. *See, e.g.,* Takimoto et al.: Clinical applications of the camptothecins. *Biochemica et Biophysica Acta 1998,* 1400: 107-109 (in particular, see page 108 and Table 3, page 112). Indeed, the Office Action admits that "comptothecin compounds are well known to have utility in treating a variety of cancers." *See* September 4, 2008, Office Action, p. 3.

Moreover, Applicants have provided experimental results demonstrating anti-cancer activity for a number of the claimed compounds. *See* Example 17. Applicants submit that once anti-cancer activity is demonstrated for these compounds (camptothecins), those of ordinary skill in the art would be able to follow routine procedures to develop that compound into a wide spectrum anticancer drug. *See, e.g.,* Clemento: New And Integrated Approaches To Successful Accelerated Drug Development. *Drug Information Journal 1999*, 33:699–710.

Accordingly, undue experimentation would not be required to practice the invention described in claims 99-108. Although claims 99-108 are directed to the full range of cancers, those of ordinary skill upon reading the present application as filed would have expected the claimed compounds—which applicants discovered were topoisomerase I inhibitors—to have activity against a wide range of cancers. Thus, one skilled in the art, based on the disclosure provided by the Applicants in view of the knowledge provided by the prior art, would be able to develop the claimed compounds (topoisomerase I inhibitors/anti-cancer compounds) into a wide spectrum anticancer drug without undue experimentation. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Withdrawal of the Section 112, first paragraph, rejection is respectfully requested.

*Discussion of the Indefiniteness Rejection*

The Office Action rejects all of the pending claims (claims 55-108) under 35 U.S.C. § 112, second paragraph, for the use of the allegedly indefinite claim term "derivatives." The Office Action points to an alleged absence of a definition for the term "derivatives" and suggests that the term be deleted from the claims.

While Applicants disagree with the allegation that the claim term "derivatives" renders the claims indefinite, Applicants have amended the claims by replacing the term

"derivative" with "compound." Applicants respectfully submit that the indefiniteness rejection is moot, and should be withdrawn.

*Discussion of the Obviousness Rejections*

Claims 59, 61, 62, 64-76 and 79-96 are rejected as allegedly obvious over the Du publication in view of the Cao '943 patent, the Cao '239 patent, and the Wall patent. Applicants respectfully disagree with the Office Action.

Contrary to the suggestion in the Office Action, those skilled in the art would have had no motivation to initially select the prior art compound of Du, let alone be motivated to modify the compound of Du in a manner which would have provided the invention as claimed. More specifically, those of ordinary skill in the art had no motivation to select as a lead compound and then to modify 10-hydroxy-camptothecin (compound 5) of the Du publication to di-ester compounds.

The Du publication discloses 10,20-diacetate derivatives of camptothecin and its C-7 *t*-butyldimethylsilyl analog (compounds 6-9), but teaches these compounds to have utility only as synthetic intermediates in the semisynthesis of the desired product 7-*tert*-butyldimethylsilyl-10-hydroxy camptothecin, *i.e.,* DB-67. Further the Du product, DB-67, is a 10,20 di-*hydroxy* camptothecin, and not a di-ester camptothecin as required by the pending claims. Based on the teaching (or, more correctly, the lack thereof) concerning the properties and uses for the intermediate, and the fact that the ultimate compound is not a di-ester, there is no motivation provided thereby for one skilled in the art to select this intermediate for further development as a stand-alone compound. The obviousness rejection fails for this reason alone. There simply is no rationale suggested for why a di-ester compound should have been made based on the activity of DB-67.

Assuming one skilled in the art would somehow select a compound disclosed in Du for further development, nothing within the disclosures of the Cao and Wall references suggests the desirability of modifying the di-acetate intermediates of Du so as to arrive at the 10, 20-diester 10-hydroxycamptothecin compounds described in the pending claims, nor any disclosure which provides any indication that such a modification would be reasonably expected to yield a useful compound. Indeed, the sole motivation to make the aforesaid modification is hindsight.

The pending application, in fact, identifies uncertainties associated with the modification of compounds via carboxylesterases/hydrolysis. Specifically, paragraph [0029] of the current application notes that the consequence of carboxylesterases/hydrolysis includes both the activation of prodrugs and the *deactivation* of drugs. (The pending application discloses that esterases are useful in the preparation of the claimed compounds.) Thus, even if one accepts the teaching of the Cao or Wall references, one skilled in the art would not have a reasonable expectation that a modification of the 10, 20-diacetate intermediates of Du would provide a compound having any activity at all, much less possess all of the advantages provided by the inventive compounds, *e.g.,* retention of activity and lower toxicity relative to the prior art 10-HCPT compound. Such reasonable expectation is not provided by the prior art.

The cited prior art further fails to teach or suggest the inclusion of the claimed compounds in the claimed compositions, or use of these compounds in the methods as claimed.

For at least the foregoing reasons, Applicants respectfully request that the obviousness rejection of claims 59, 61, 62, 64-76 and 79-96 be withdrawn.

*Conclusion*

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

/Christopher T. Griffith/

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